[CHAPTER 5]

Assessing Pesticide Risks

The mission of DPR is in essence to ensure that people and the environment are protected from adverse effects that may be associated with pesticide use. Determining what those effects might be and under what circumstances they can occur is essential to an effective regulatory program. When this information is known, measures can be taken to limit exposures so that adverse effects can be avoided.

This chapter discusses the process DPR uses to assess pesticide risk, that is, to estimate the likelihood that an adverse health effect will result from an exposure (or exposures) to a particular amount (dose) of a pesticide or pesticides. *Risk assessment* is a process designed to answer questions about how toxic a chemical is, what exposure results from its various uses, what is the probability that use will cause harm, and how to characterize the risk.

Toxicity is an inherent property of all substances; all chemical substances can produce adverse health effects at some level of exposure. Risk of adverse health effects is a function of toxicity and exposure. Exposure to a substance determines the dose and the substance's toxicity determines the potency of the dose. Therefore, determining both toxicity and exposure is necessary in assessing the risk of chemicals. An extremely toxic substance is of little concern if there is no exposure to it. On the other hand, a moderately toxic chemical to which many people are exposed creates a substantial potential risk to human health. Hazard is best defined as the potential of a substance to cause harm, whereas risk is the probability of adverse effect under specified conditions of exposure. Regulatory agencies use various experimental data to determine the conditions likely to result in toxic effects, and use that information to set exposure doses which are reasonably expected to cause no adverse health effects. Once the risk has been assessed and characterized, risk managers decide if and how any unacceptable risk of harm can be reduced to an acceptable level. The results of risk assessments are often the driving force behind new DPR regulations and use restrictions.

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Brief History of Risk Assessment: Since the late nineteenth century, risk assessment and risk management have been everyday activities of many industries, including banking and insurance. In the early twentieth century, the principles of risk assessment began to be applied to human health and safety and by the 1940s, toxicologists began to study the problem of establishing limits on exposures to hazardous substances that would protect human health. The impetus to better assess safety of chemical exposures took on new urgency in the decades that followed, as it became apparent that long-term exposures could have chronic health implications. The Congressional passage in the 1970s of landmark environmental and occupational safety legislation raised the importance of risk analysis and led to efforts to systematize general procedures and policies and formalize quantitative methodologies.

In California, the focus on pesticide risk assessment grew out of the 1984 passage of the Birth Defect Prevention Act *(BDPA, see separate article in this Chapter)*. The BDPA mandated that the State bring the toxicological database on pesticides (based on required studies) up to current scientific standards, determine if the studies identified adverse health effects, and determine if those health effects were significant. These determinations are made through the risk assessment process. These mandates prompted the 1985 creation of the Medical Toxicology Branch to evaluate toxicological data and conduct risk assessments.

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Birth Defect Prevention Act

In 1984, the Legislature passed the Birth Defect Prevention Act (BDPA, Chapter 669, SB 950). The law required that DPR not register new active ingredients without a full complement of health effects studies, and mandated that registrants of older pesticides (those registered before 1984) bring health effects data on their chemicals up to current scientific standards. The studies (primarily done on experimental animals) were in the following areas: chronic toxicity, mutagenicity, neurotoxicity, oncogenicity, reproductive effects, and teratology. The BDPA required DPR to use these and other data to determine if a pesticide would cause human health problems. If continued use of a pesticide presents a significant health hazard that cannot be mitigated, DPR is required to cancel the registration of products containing that active ingredient.

The BDPA mandated that DPR begin by determining 200 active ingredients that would be the first focus of enforcement. The priority list included chemicals with the most significant data gaps, widespread use, and which were suspected of being of greater health concern. (A data gap means that DPR lacks adequate health effects studies in any one of the required categories listed above.)

In January 1986, DPR notified registrants of data gaps for pesticide products containing any of the 200 priority active ingredients. DPR found that much of the data submitted in response to the data call-in notice did not meet U.S. Environmental Protection Agency guidelines. Because these studies had been performed some years before, many registrants were unable to obtain additional data from the laboratories that conducted the original studies. Registrants then contracted with laboratories to begin new studies; however, most registrants failed to complete and submit new chronic health effects studies within the time frames set by the law. The BDPA required submission of data on priority-list pesticides by March 1991, a deadline the Legislature later extended to March 1996 (Chapter 1228, Statutes of 1991, SB 550). Subsequent legislation (Chapter 1, Statutes of 1995-1996, SB 1XXX) extended until December 1997 the data deadline for two pesticides, methyl bromide and pentachlorophenol.

By the end of 2000, 55 of the 200 priority active ingredients had either been withdrawn from the market by their manufacturers or been suspended by DPR for failure to submit required data. (Product registrations are suspended if data for any active ingredient cannot be upgraded with the submission of additional information or if data were not submitted.) Of the 145 remaining, adequate data had been received for 142 (including required studies for methyl bromide and pentachlorophenol). Pesticide registrants are in compliance with the BDPA when DPR receives all required studies, unless later evaluation by DPR scientists determines that any study is not adequate. For the three active ingredients not in compliance, studies for one were under review for adequacy, and exemptions had been granted for products containing the other two. (Under the BDPA, a pesticide may be exempted from the data requirements if it is determined the chemical has only limited use, and there is insignificant exposure to workers or the public.)

In 1992, DPR began the process of calling in data for the 703 registered active ingredients that were not on the priority list, under a timetable set by 1991 legislation (Chapter 1227, AB 1742).

By the end of 2000, there were 538 active ingredients no longer subject to data requirements. These active ingredients had been withdrawn from the market by the manufacturers, were suspended by DPR, or were not subject to BDPA data requirements (for example, spray adjuvants). Of the remaining 165 active ingredients, 127 had complete data on file and four were exempt. Another nine were at various stages in the process. (Requests were received for waivers or exemptions, which the BDPA allows for those chemicals with insignificant exposure potential.) The remaining five active ingredients are subject to suspension.

Once a pesticide registration is suspended, registrants must halt all sales. Retail dealers may continue selling affected products for two years, and consumers may continue to use products on hand.

DPR scientists continue to evaluate health effects data submitted by registrants to confirm that studies were conducted properly and that chemicals registered on the basis of those studies can be used safely in California.

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To fulfill the mandates of the BDPA, DPR established a procedure to prioritize all pesticides for risk assessment, placing them in high, moderate, or low-priority status. (The priority status was and continues to be determined by DPR's Adverse Effects Advisory Panel, which includes senior scientists from the Worker Health and Safety and Medical Toxicology branches, and Cal/EPA's Office of Environmental Health Hazard Assessment [OEHHA]). Prioritization is based on the nature of the potential adverse health effects identified in toxicity studies, number of potential adverse health effects, number of species affected, potential for human exposure, use patterns, amount of pesticide used, U.S. EPA evaluations and actions, and similar factors. Using these criteria, the panel prioritizes the pesticides for risk assessment, based on their potential for health problems.

Furthermore, DPR policy from the 1980s through 1996 called for completion of a full risk assessment before any new, high-priority pesticide active ingredient could be registered in California. (New active ingredients that were classified as moderate or low priority for risk assessment were allowed to proceed through the registration process after an evaluation but without a risk assessment.)

Under this policy, older chemicals registered before the passage of the BDPA were prioritized separately, and placed on a different risk assessment track. This bifurcation of effort slowed risk assessments for older chemicals that had been registered sometimes decades before, when risk evaluations were nonexistent or abbreviated, and at the same time delayed registration of new pesticides.

In 1996, DPR instituted a new policy integrating its risk assessment tracks. U.S. EPA extensively reviews new pesticide active ingredients before federal registration, using up-to-date toxicology data. On that basis, DPR policy now allows an active ingredient to be registered in California after an evaluation but without a risk assessment, providing all required toxicology and other data have been submitted. The newly registered active ingredient then goes to DPR's Adverse Effects Advisory Panel for prioritization.

Pesticides are now placed on a single priority list for risk assessment, allowing DPR to better focus its resources on pesticides that pose the highest potential risk.

> ***It is more important to keep worthless or hazardous products off the market than to attempt to run down and catch those selling such materials after they have already made sales.***
> *– 1946 Department annual report*

The Risk Assessment Process

Risk assessment can be broken down into four steps:

- hazard identification
- dose-response assessment
- exposure assessment
- risk characterization
- risk appraisal

Hazard identification involves the review and evaluation of a pesticide's toxic properties — the extent and type of adverse effects. This phase, conducted primarily by DPR's Medical Toxicology Branch, usually involves gathering data on whether exposure to a chemical causes an increased incidence of an adverse effect (for example, cancer or birth defects in experimental animal studies). This is usually determined by a battery of studies on several species of laboratory animals.

Hazard identification also determines whether it is scientifically correct to infer that adverse effects observed in one species will occur in other species; for example, whether substances found to cause tumors or birth defects in experimental animals are likely to have the same effect on humans. Evaluation may also involve characterizing behavior of a chemical within the human body and chemical interactions within organs, cells, or even parts of cells.

The **dose-response assessment** considers the effects (in terms of magnitude and/or incidence) that occur or are predicted to occur at a given dose level. State and federal guidelines require that laboratory animals receive doses sufficient to produce toxic effects. These tests often use doses which are much higher than those to which people might be exposed. The highest dose in a study which does not result in an observable effect (that is, the dose below the dose at which an effect was seen) is called the "no-observed-effect level" (NOEL). This NOEL is often the basis for calculating allowable human exposures. To compensate for inevitable uncertainties in the risk assessment process, various uncertainty factors may be applied to the NOEL to determine the allowable exposure level. (For example, the allowable human exposure may be set a hundredfold lower than the NOEL. The first safety factor of 10 allows for possible differences between how humans and animals might react to a chemical. The second safety factor of 10 takes into consideration that some humans are more sensitive than others.)

Of equal importance with hazard identification in assessing risk is **exposure assessment**, which estimates people's potential exposure to a chemical at work and at home, in air and from water and food in their diets. The process involves specifying the population that might be exposed (looking at various subpopulations by occupation, age, gender, ethnicity, and other factors), identifying the routes through which exposure can occur (skin, inhalation, ingestion), and estimating the magnitude, duration, and timing of the doses that people might receive as a result of their exposure. *(See Chapter 6 for more information on DPR's exposure assessment process.)*

Risk characterization integrates data from hazard identification, dose response and exposure assessments to develop a qualitative or quantitative estimate of the likelihood that any of the hazards associated with the pesticide will occur in exposed people. These evaluations offer estimates of risk or margins of safety. **Risk appraisal** describes the significance and uncertainties of the risk characterization.

DPR prepares a **risk characterization document (RCD)** for each pesticide that goes through this process. The RCD explains the results of the risk assessment. The risk characterization document assembles, critiques and interprets all pertinent scientific data on a chemical's toxicology, human experience, and exposure.

An initial RCD draft undergoes internal departmental review by DPR scientists. The RCD then undergoes external peer review by scientists at OEHHA and U.S. EPA. DPR may also call upon other scientific experts for additional external peer review. External peer review provides critical information for DPR on the scientific completeness of its documents. DPR considers the comments from these reviews and makes changes as appropriate. As new data become available, DPR updates the RCD with appendices. Sometimes, the entire RCD may be rewritten if new information substantially changes the conclusions.

The final step, separate from the risk assessment process, is **risk management**, when regulators decide how much exposure to a given chemical will be allowed and (if necessary) evaluate and select risk reduction options. If estimated risk falls within acceptable parameters, including a margin of safety, DPR allows use (or continued use) of the pesticide. If estimates suggest an unacceptable level of risk (that is, an unacceptable safety margin), exposure mitigation measures (that is, risk reduction options) are explored, since exposure is the controllable aspect of risk or margin of safety. In determining mitigation strategy, DPR must consider effectiveness, practicality, and enforceability of mitigation measures. Exposure may be reduced by changes in chemical formulation and/or packaging, personal protective equipment and clothing, engineering controls, and restrictions on use of a chemical, among other options. The effects of any proposed mitigation measures are run through the risk assessment process again, to determine if they will result in sufficient exposure reduction.

Unlike risk assessment, risk management is not based solely on scientific considerations, since it also involves social, economic, and legal considerations to make regulatory and policy decisions. DPR considers these factors in analyzing the possible regulatory responses to potential health hazards. The process is necessarily subjective in that it requires value judgments on the acceptability of risks and the reasonableness of control measures. However, the crucial point is simple: DPR will not allow a chemical to be used unless it can be used safely. If risk management measures are inadequate, then a pesticide registration may be suspended, canceled, or denied.

> "Risk assessments have many uses, but a major one is to assist decision makers with the complex choices regarding the options in managing or reducing the potential human health risks associated with a substance or product. Risk management is defined in the US as the process of evaluating alternative regulatory actions and selecting among them. It has been characterized as an agency decision-making process that entails consideration of political, social, economic, and engineering information along with risk-related information to develop, analyze, and compare regulatory options and to select the appropriate regulatory response to a potential health hazard . . . . Using experience and judgment, the (risk) manager must determine a level of risk that is acceptable."
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> *– Risk assessment, risk evaluation, and risk management, C.J. Henry (in Food Safety and Toxicity)*

Proposition 65

In 1986, California voters passed a ballot initiative called "The Safe Drinking Water and Toxic Enforcement Act," more familiarly known by its original name, Proposition 65. Among other mandates, the Act requires the State to publish a list of chemicals "known to the State to cause cancer or reproductive toxicity," and to update this list annually.

A chemical may be listed if:

- State experts conclude that scientifically valid testing shows the chemical clearly may cause cancer or reproductive toxicity;
- if an authoritative body has formally identified it as causing cancer or reproductive toxicity; or if an agency of the State or federal government has formally required it to be identified as causing cancer or reproductive toxicity.

Twelve months after a substance is added to the State's Proposition 65 chemical list, businesses with ten or more employees must provide a warning before knowingly and intentionally exposing their employees or the public to an amount of the listed pesticide that poses a significant risk. The warning must be "clear and reasonable." Also, 20 months after a pesticide is listed, businesses must not knowingly discharge listed pesticides, in a concentration that poses a significant risk, into drinking water or onto land where it will pass or probably will pass into a source of drinking water. Prohibitions do not apply if exposures to listed carcinogens result in "no significant risk," or if exposure to listed reproductive toxicants is less than 1/1,000th of the no-observed-effect level, or NOEL.

The Governor designated Cal/EPA's Office of Environmental Health Hazard Assessment (OEHHA) as the lead agency for implementation of the Act. DPR's Proposition 65 role is limited to conducting scientific evaluation of pesticides being considered for listing. In cases where a given chemical has both pesticidal and major nonpesticidal uses, DPR and OEHHA share responsibility.

DPR's Medical Toxicology Branch reviews data regarding possible adverse health effects (carcinogenicity, reproductive and developmental toxicity, and genotoxicity) of pesticidal chemicals to assist OEHHA in determining when pesticides should be listed.

DPR's hazard communication regulations (which govern pesticide and worker safety requirements) also provide a foundation for employers to meet the Proposition 65 warning requirements for employees in the pesticide workplace. Proposition 65 regulations also allow warnings to be provided in the same manner stated in the federal Hazard Communication Program regulations for workplace exposures.

California's hazard communication program requires that, whenever employees are working in treated fields or handling pesticides, the employer must display certain leaflets in the Pesticide Safety Information Series (PSIS) produced by Worker Health and Safety Branch. The leaflets are available in both English and Spanish and must be read upon request to any employee. In addition, specific information on an application must be displayed at a central location within 24 hours of the application and remain for 30 days or until employees are no longer present, whichever occurs earlier.